Basal Ganglia

***Anatomical considerations*: Fig.1**

The term “basal ganglia “is generally related to 5 structures:

A. THERE LARGE NUCLEAR MASSES

1. Caudate
2. Putamen
3. Globus Pallidus (divided into an external and internal segments).

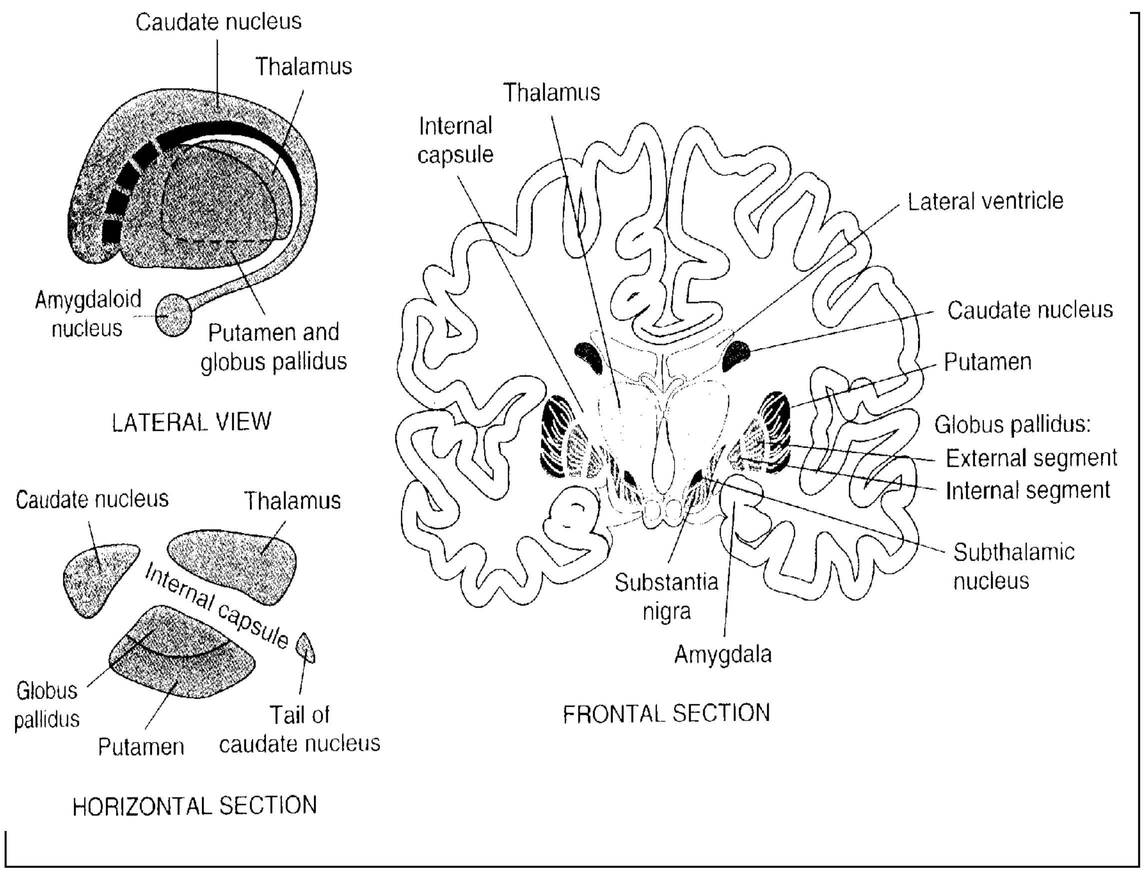

FIG. (1): **THE BASAL GANGLIA**

B. FUNCTIONALLY RELATED NUCLEI

1. Subthalamic nucleus.

2. Substantia nigra (divided into pars compact and pars reticulata).

N.B: **Fig.2**

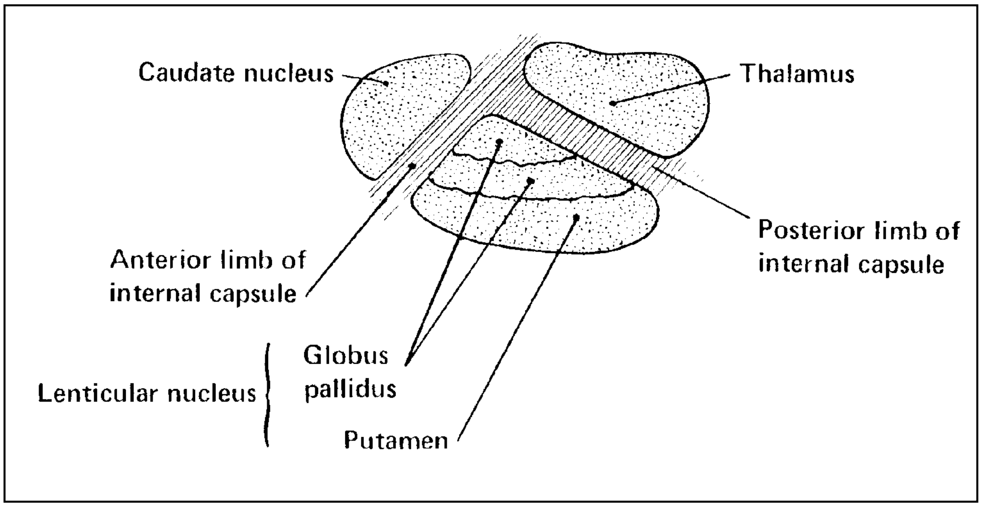

FIG. (2): **LATERAL VIEW OF BASAL GANGLIA AND ADJACENT STRUCTURES**

- Caudate + putamen are called “striatum”
- Putamen + globus pallidus are called “lenticular nucleus”

Neuronal connections and neurotransmitters of the basal ganglia:

Functionally important pathways connect the nuclei of the basal ganglia with each other and with other areas of the nervous system.

The main connections are:

(1) Internal connections:

The caudate and putamen are regarded as the receiving center of the basal ganglia, while the globus pallidus is the discharging center. The most important internal connections are:

i. Striato-Pallidal projection:

This starts from the caudate and putamen to the globus pallidum, secreting the inhibitory transmitter GABA.

ii. Striato-nigral projection:

Axons from neurons in the neostriatum (caudate & putamen) pass to the substantia nigra pars reticularis and secrete GABA.

iii. Nigro- Striatal projection:

Axons from substantia nigra pars compacta to the striatum, secreting dopamine which may be excitatory (D1) or inhibitory (D2) according to the receptor.

iv. The interneurons of the striatum: secretes acetyl choline, which may be inhibitory or excitatory according to the receptors.

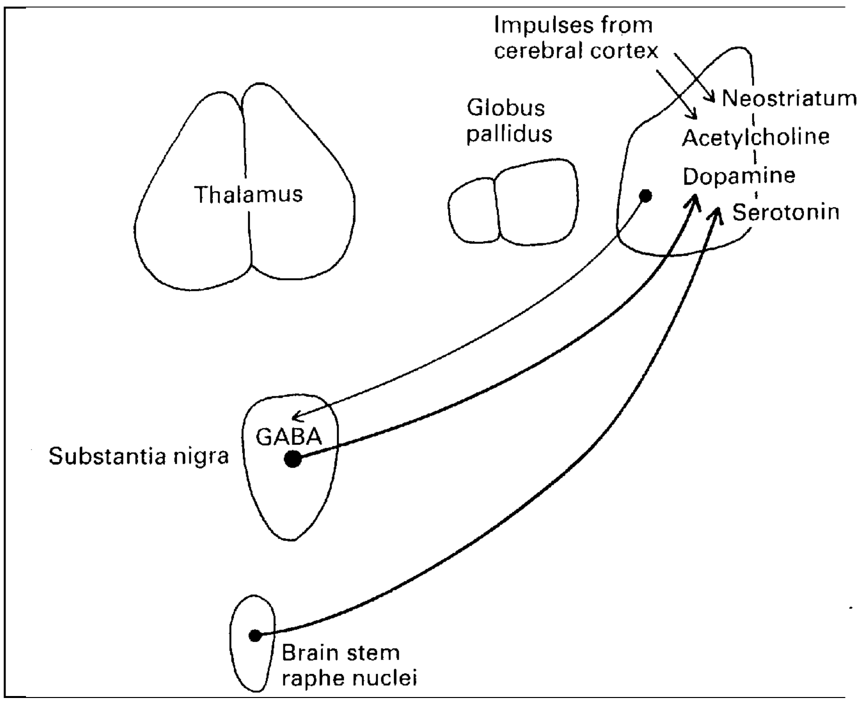

Fig. (3): *Afferent and efferent pathways of the neostriatum showing several transmitter substances: glutamate in corticostriatal endings, GABA in the substantia nigra and globus pallidus, and dopamine and scrotonin in the neostriatum.*

(2) Cortical connections:

- The Basal Ganglia receive excitatory input from many **cortical areas** through the neurotransmitter **Glutamate** to the striatum.

It then processes this information through the direct and indirect pathways.

<u>i.The direct pathway:</u>

- The **Cortex** sends excitatory fibers to the **striatum**.

- The striatum **then inhibits the internal segment (IS) of the Globus Pallidus** using the neurotransmitters **GABA.**

- When the globus pallidus (IS) is inhibited, it **cannot inhibit** the **Thalamus** rendering it free to fire and sends **excitatory** input up to the Cortex, which **<u>facilitates movement</u>**.

<u>ii.The Indirect Pathway</u>

- The **Cortex** sends excitatory fibers to the **striatum**.

- Then striatal neurons send inhibitory input to the **external segment of the Globus Pallidus** using the neurotransmitters **GABA.**

- The Globus Pallidus external segment is *unable to inhibit the Subthalamic* nucleus leaving it free to fire.

- **The Subthalamic Nucleus** being uninhibited sends the only purely **excitatory input** within the Basal Ganglia pathways **to the Globus Pallidus internal** segment**.**

- Globus pallidus (IS) then **inhibits the VA and VL of the Thalamus** making it unable to send excitatory input to the Cortex and thus indirectly inhibiting the Motor Cortices, which **<u>inhibits movement.</u>** The balance of usage of the direct versus the indirect pathway is how the Basal Ganglia are involved in the control of movement.

- **Dopamine,** secreted from substantia nigra to the striatum.

- It acts primarily through dopamine **D1** receptors on the neurons that participate in the **direct pathway, exciting** these neurons.

It acts on dopamine **D2** receptors on the striatal neurons that are involved in the **indirect pathway**. The D2 receptors are **inhibitory.** Therefore, dopamine excites the direct pathway and inhibits the

indirect pathway, with a net effect to increase facilitatory inputs to the motor regions.

(3) <u>Efferent pathway from the basal ganglia</u>: **Fig.5**

- The globus pallidus external segment projects to subthalamus and brain stem nuclei, secreting the inhibitory transmitter GABA. From these areas fibers pass to the reticular formation and sends impulses via the extrapyramidal tracts (reticulospinal, vestibulospinal and rubrospinal tracts) to the motor neurons of the spinal cord.
- The globus pallidus internal segment axons secrete GABA to the thalamus (ventrolateral and venrto anterior nuclei) and then to the cortex.

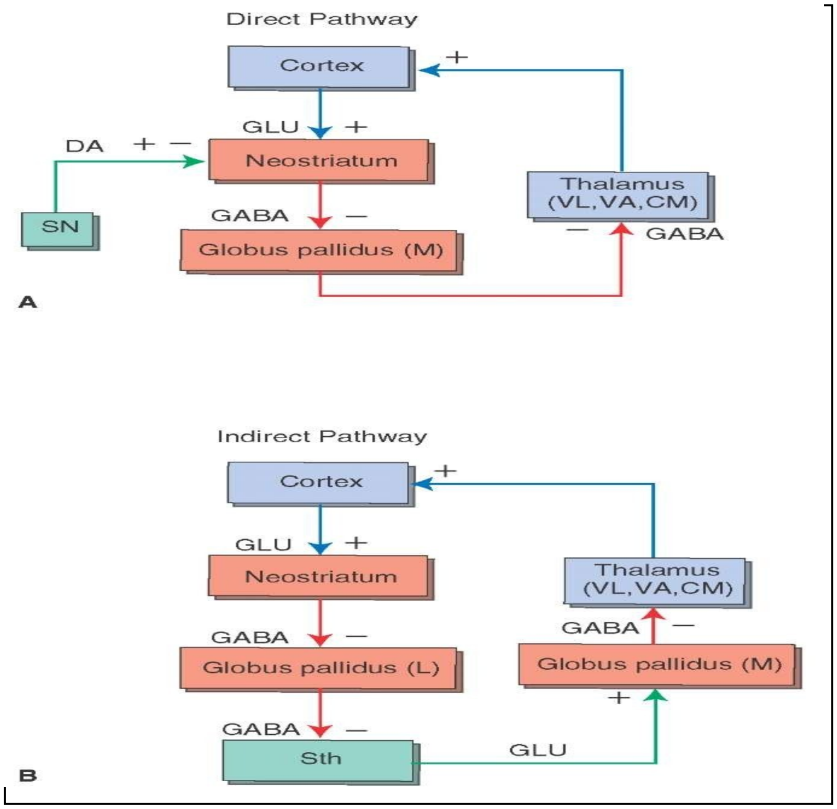

Fig. (4): *Afferent and efferent pathways of the direct (A) and indirect (B) pathways showing several transmitter substances: glutamate in corticostriatal endings, GABA from the neostriatum and globus pallidus, and dopamine from the substantia nigra.*

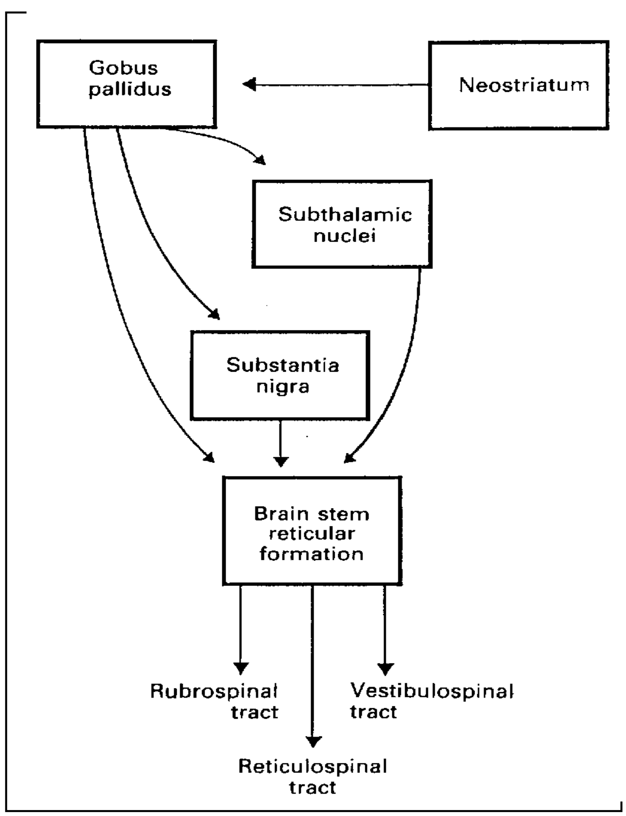

Fig. (5): *Diagram showing the main different pathways from the basal ganglia to the brain stem reticular formation*

N.B.

1. Physiological significance of most of the above neural connections is still uncertain.
2. Normal function of the basal ganglia is brought about by a balance between the various excitatory and inhibitory influences of the various transmitters.

Functions of the basal ganglia:

- Neurons in the basal ganglia discharge before movements begin. This observation led to the idea that the basal ganglia are involved in the planning and programming of movement or, more broadly, in the processes by which an abstract thought is converted into voluntary action.
- It is thought that the Basal Ganglia work as a gate in allowing the initiation of voluntary movements. These voluntary movements are viewed as motor programs that are stored in the Motor cortices.
- The Basal Ganglia facilitates the appropriate motor program for a task by exciting the cortex using the direct pathway and inhibits other competing motor programs by inhibiting the cortex using the indirect pathway.

The basal ganglia play a very important role in motor control. The most important functions include:

1. The ***caudate nucleus,*** is involved in **cognitive** control of motor activity which means using of thoughts and information stored in the memory for selection of an action, modifying the ***timing*** i.e. they can occur rapidly or slowly, and also modifying the ***spatial dimensions*** e.g. one can write very small or very large letter, e.g.

when one is subjected to a danger, he responds immediately by turning away from it then begins to run.

2. The putamen circuit helps the corticospinal system in executing subconscious learned patterns of movement such as writing letters of the alphabet, cutting with scissors and some aspects of vocalization.
3. The basal ganglia are also responsible for initiation and regulation of the gross intentional movements of the body e.g. swinging of the arms while walking and facial expressions.
4. The globus pallidus is thought to be responsible for the posture taken by the body to perform a particular voluntary movement i.e. it locks the different parts of the body into a specific position so as to facilitate the fine movements of the hand.
5. The basal ganglia are mainly inhibitory to the muscle tone.

Diseases of the basal ganglia in human:

[1] Chorea:

- Due to: Lesion in the caudate and putamen.
- As a complication of a hereditary disorder, known as Huntington's chorea.
- As a complication of rheumatic fever in children.

It is characterized by:

1. Spontaneous, rapid, involuntary dancing movements.
2. Hypotonia associated with pendular knee jerk.

Mechanism of the disease:

- The mechanism behind the abnormal movements of chorea is not clear. However, it is proposed that the loss of most of the cell bodies of

the GABA-secreting neurons in the caudate nucleus and putamen of the indirect pathway interrupts the negative feed back loop from basal ganglia to cortex → leading to abnormal movements.

[2] Athetosis:

- ***Due to:*** Lesion in globus pallidus.
- ***Pathology:*** Wilson's disease
    - ***<u>N.B.</u>***
    - Substantia nigra has high content of copper. In Wilson's disease where ceruloplasmin is low, there is chronic copper intoxication and degeneration of lenticular nucleus.

- ***Characterized by:*** Continuous, slow writhing (worm-like) movements of the hands, arms, neck and face it is associated with hypertonia.

[3] Ballism:

- ***Due to:*** Lesion in subthalamus.
- ***Pathology:*** vascular lesion.
- ***Character:*** Involuntary movements that is flailing, intense and violent.

[4] Parkinsonism:

- ***Due to:*** Lesion in substantia nigra.
- ***Pathology:***

a. Cerebral atherosclerosis: loss of dopamine receptors.

b. Head trauma.

c. Phenothiazine drugs which block D_2 dopamine receptors.

Mechanism of disease:

Recently pathogenesis of Parkinson's disease is attributed to the fact that there is imbalance between excitation and inhibition in the basal ganglia, created by the loss of the dopaminergic inhibition of the putamen.

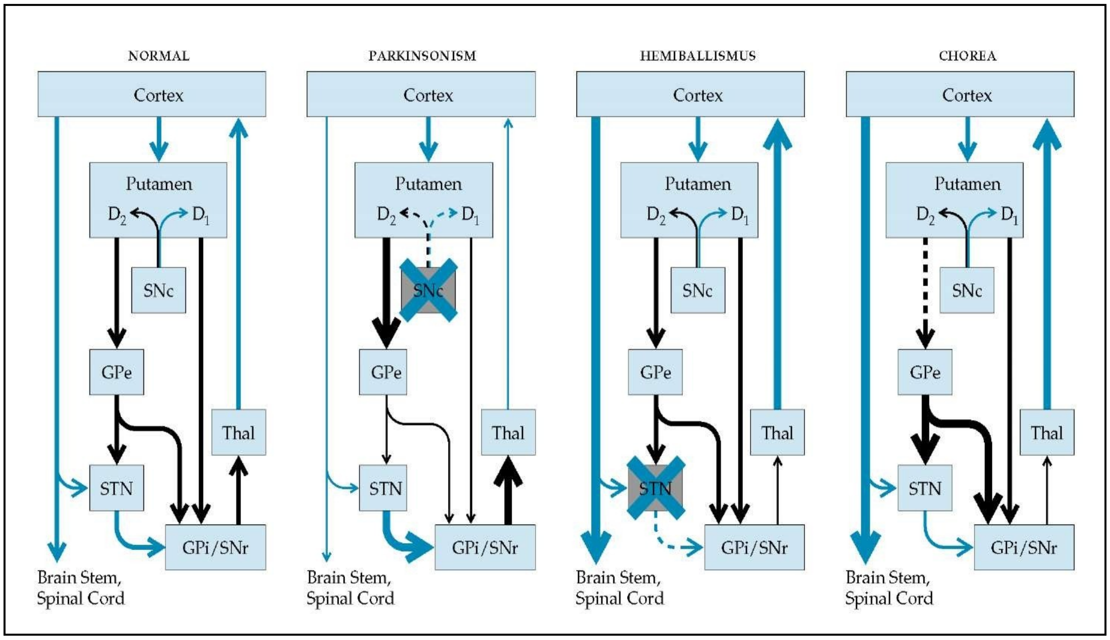

Fig. (6): *Diagram showing the mechanisms and the pathways involved in cases of parkinsonism, hemiballismus and Chorea.*

Characters:

1. Rigidity:

- ***Affected muscles:*** Both flexor and extensor muscles are affected. However, flexors are affected more, so the patient develops a *generalized flexion attitude*.
- ***Type:*** Lead-pipe rigidity i.e. there is a continuous resistance to bending throughout the range of movement. Sometimes, there is a series of catches during passive movement "*Cogwheel Rigidity*".
- ***Mechanism:*** Rigidity is due to excess impulses transmitted along the corticospinal tract to both alpha AHC_s and gamma $ACH_{s.}$

2. Tremors: Static Tremors:

- ***Def:*** It is rhythmic involuntary alternating contractions of the antagonistic muscles.
- ***Characters:*** present at rest and disappears with activity occurs in the form of pill rolling movement at the hand and or up and down movement of the mandible.

3. Akinesia:

- ***Def:*** It is the difficulty in initiating voluntary and spontaneous movements.
- ***Characters:***

a. Speech***:*** *monotonous*

b. *Loss of associated movements:* e.g. swinging of arms during walking.

c. Loss of facial expression i.e. *masks face.*

d. Gait: Shuffling.

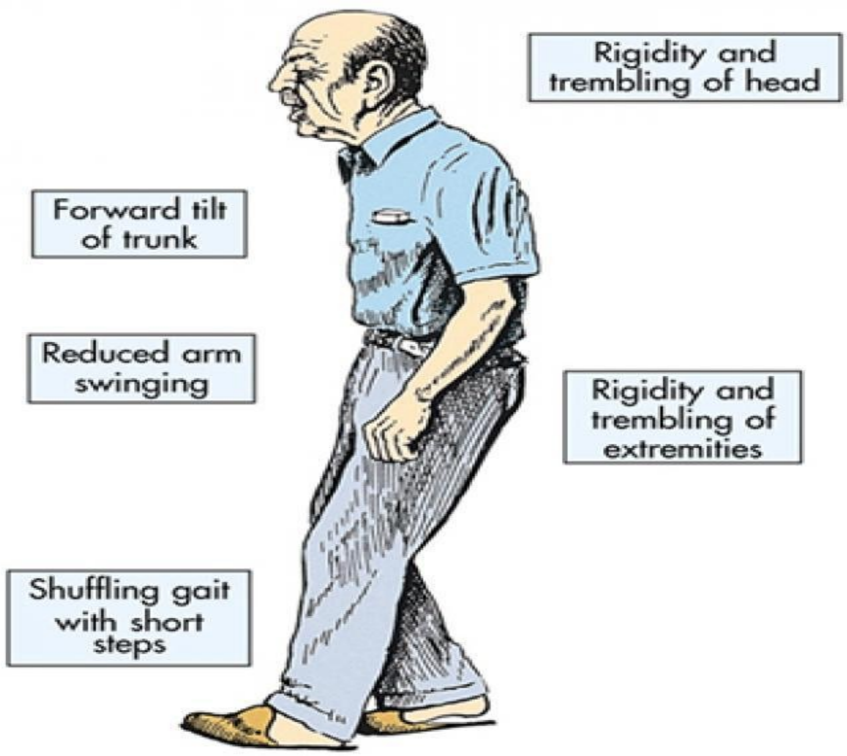

Fig. (7): *Diagram showing the main manifestations of parkinsonism.*

Treatment:

1. L-dopa (levodopa). Unlike dopamine, this dopamine precursor crosses the blood brain barrier and helps repair dopamine deficiency.
2. Anticholinergic drugs may help by decreasing the cholinergic influence.
3. Surgical treatment: by making a lesion in the internal segment of the globus pallidus (pallidotomy) or in the subthalamic nuclei may help to restore the output balance toward normal.
4. Implantation of dopamine-secreting tissue in or near the basal ganglia.